EXHIBIT 4

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Minimally Invasive versus Standard Approach in Total Knee Arthroplasty

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We compared a group of 20 patients who had 24 minimally invasive total knee arthroplasties with a similar group of 21 patients who had 25 standard medial parapatellar approach total knee arthroplasties. We wanted to clarify whether the minimally invasive group had an advantage over the standard group in muscle strength, pain level, postoperative recovery, and clinical results and whether the patients were prone to radiographically poor results, more operative time, and increased complications. The extensor and flexor torque, visual analog scale, pace of rehabilitation, Knee Society scores, radiographic findings, operative time, and complications of each group were examined. The minimally invasive group showed higher extensor torque values, higher ratios of postoperative to preoperative extensor torque, and lower average visual analog scale scores at 1 and 2 weeks. The patients in this group achieved straight leg raising, 90° knee flexion, and T-cane gait earlier. There was no component malalignment, but the tibial component shifted to a more medial position. The mean operative time was 56 minutes longer in the minimally invasive group. We encountered no major perioperative complications in either group. We believe the minimally invasive technique positively contributes to the early restoration of quadriceps strength and a speedy return to normal function.

Level of Evidence: Level III, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

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Each author certifies that his institution either has waived or does not require approval for the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.
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Minimally invasive surgery (MIS) for knee arthroplasty was introduced for unicompartmental knee arthroplasty in the early 1990s. A more rapid recovery and early return to normal function in a unicompartmental knee arthroplasty through a smaller arthrotomy has been reported.[13,14] In recent years, the techniques in MIS have been applied to total knee arthroplasty (TKA). Although the long-term results have been excellent in standard TKA, recovery from TKA is often long and painful for patients. The increasing interest in MIS among patients and orthopaedic surgeons has been a driving force in the development of MIS TKA.

Minimally invasive surgery for TKA is less invasive for the extensor mechanism with minimal disruption of the quadriceps muscle and is performed without eversion of the patella.[1–4,8,11,17] Minimally invasive surgery for TKA that avoids incision into the quadriceps tendon or the vastus medialis is reported to result in less pain perioperatively, a greater range of motion (ROM), and a shorter length of hospital stay than a standard TKA.[2,4] In addition, MIS TKA through a mini-midvastus approach has been reported to lead to earlier improvement of ROM and higher Knee Society scores than a standard TKA.[8,11] These reports suggest techniques that avoid disruption of the extensor mechanism and eversion of the patella result in more rapid recovery of knee function compared with traditional TKA exposures. To date, no English literature has evaluated quadriceps strength quantitatively and objectively. Furthermore, most of the current evaluations of MIS TKA so far reported are merely radiographic evaluations of implant alignment.[2,8,11]

We wanted to clarify whether MIS TKA had an advantage over the standard medial parapatellar approach TKA in terms of muscle strength, pain level, rate of postoperative recovery, and clinical scores. Furthermore, we wished to determine whether patients who had MIS TKAs were prone to radiographically poor results, more operative time, and increased complications.

TABLE 1. Preoperative Data

Parameter	MIS TKA	Standard TKA
Number of patients	20	21
Number of TKAs	24	25
Number of men	2	2
Number of women	18	19
Age (years)	76.1 (range, 65–86)	73.9 (range, 62–86)
Height (cm)	147.7 (range, 133.8–167.0)	151.4 (range, 140.0–159.0)
Weight (kg)	55.0 (range, 36.5–74.0)	59.5 (range, 43.0–75.9)
Extension (°)	8.1 (range, 0–15)	8.0 (range, 0–30)
Flexion (°)	122.3 (range, 90–150)	118.4 (range, 60–150)
Knee score	38.8 (range, 1–68)	37.7 (range, 0–63)
Functional score	46.0 (range, 5–70)	40.8 (range, 5–70)
Radiographic stage (Kellgren and Lawrence[10])	Grade 4: all	Grade 4: all

MIS = minimally invasive surgery

MATERIALS AND METHODS

Between December 2004 and July 2006, 24 MIS TKAs (Legacy® LPS-Flex; Zimmer, Warsaw, IN) in 20 patients were performed for osteoarthritis. A capsular incision only was used in eight knees, whereas an additional 1 to 2 cm of vastus medialis oblique (VMO) snip was used in 16 knees. The patients were randomly selected for MIS surgery unless they previously had an osteotomy or had severe osteoporosis. The standard group included 25 TKAs (23 Legacy® LPS and two LPS-Flex; Zimmer) in 21 patients during the same period using a standard medial parapatellar approach. The mean length of followup was 16 months (range, 7–28 months) in the MIS group and 14 months (range, 7–24 months) in the standard group. The groups were matched for age, gender, body weight, preoperative ROM, Knee Society scores, and radiographic stages (Table 1).

In MIS TKA, we used an adjustable leg holder, which facilitated the repeated extending and flexing of the knee. A slightly medial straight skin incision was made from the level of the superior pole of the patella to the tibial tuberosity. The medial parapatellar retinaculum was incised and the capsular incision was extended proximally to the VMO insertion. In a patient whose VMO ran down to the distal level of the superior pole of the patella, we snipped the VMO 1 to 2 cm proximally (Fig 1). An initial patella cut was made to remove 5 to 7 mm of bone to obtain better observation. The patella was subluxed but not everted. Femoral and tibial bone cuts were made with smaller modified instruments and cutting guides, which permitted use in a small incision. Three degrees external rotation relative to the posterior condyles was established using an anteroposterior sizer, which could be aligned to the anteroposterior axis. Soft tissue balancing was performed in a standard fashion. The tibial component was cemented in place followed by the femoral and patella components. No lateral release was needed in our patients who had MIS.

On the second postoperative day, the epidural anesthesia tube and suction drain were removed and continuous passive motion was started. The patients were allowed to begin full weightbearing as soon as the pain was tolerable.

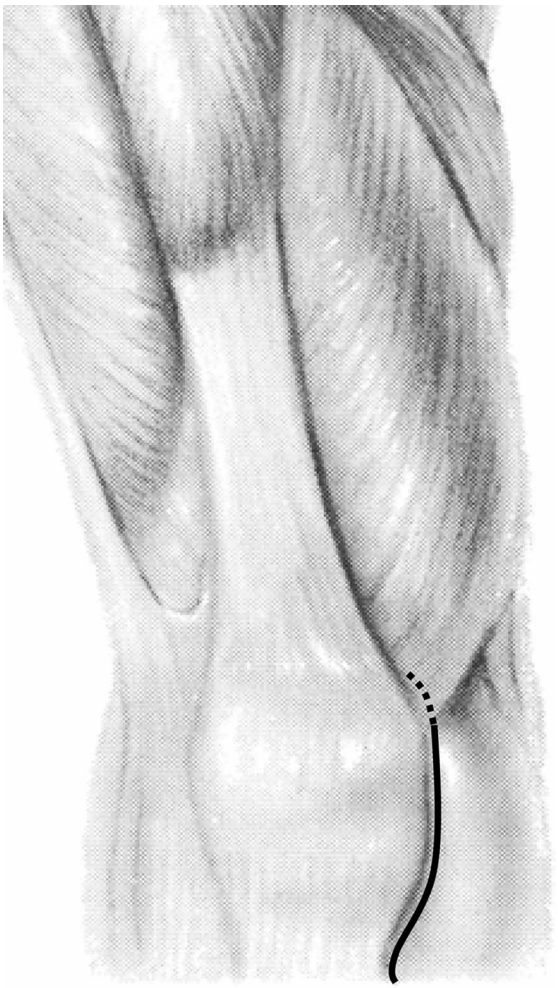

Fig 1. In MIS TKA, the medial parapatellar retinaculum is incised and the capsular incision is extended proximally to the VMO insertion (solid line). In a patient whose VMO runs down to the distal level of the superior pole of the patella, we snip the VMO 1 to 2 cm proximally (dotted line).

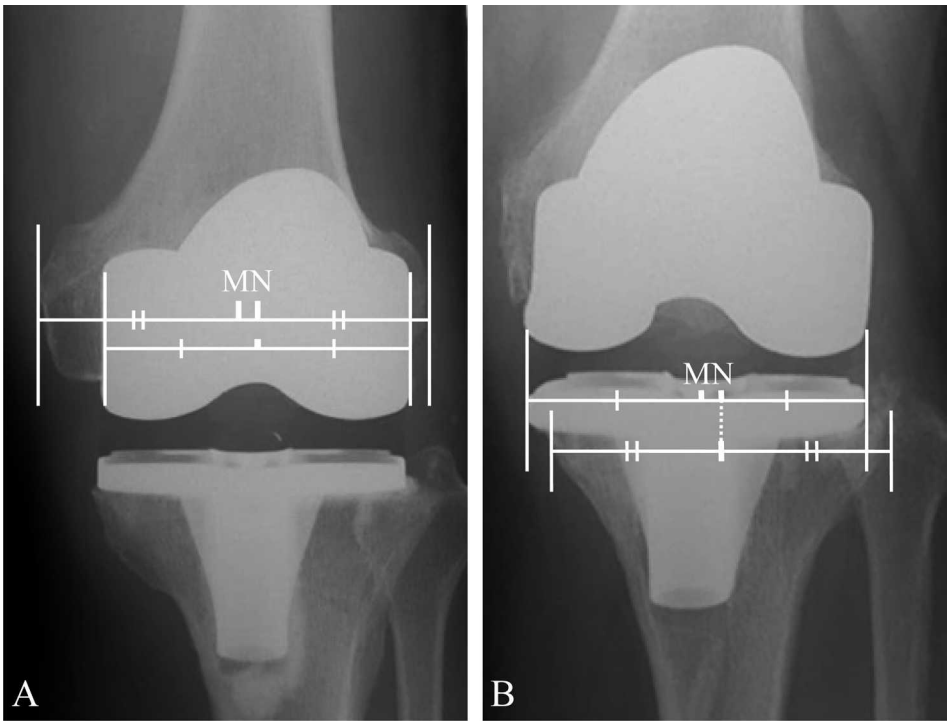

Fig 2A–B. (A) The shift length of the femoral component was measured by the distance between the midpoint of the components (N) and the midpoint of both condyles (M). (B) The shift length of the tibial component was measured by the distance between the midpoint of the components (M) and the midpoint of both condyles (N).

We measured the knee extensor and flexor torque preoperatively and postoperatively at 1 and 2 weeks using a COMBIT-CB2® (Minato Ltd, Osaka, Japan) device. The isometric torque was measured at 60° knee flexion in every patient. We evaluated the muscle torque and the ratio of postoperative and preoperative values in the two groups. The times patients could successfully perform straight leg raising, 90° knee flexion, and T-cane gait were recorded. A visual analog scale (VAS) was used to assess pain level. We also evaluated the patients using the Knee Society rating system clinically and radiographically[7,9] at 3 weeks, 3 months, 6 months, and 12 months. In addition, we estimated the shift length of the femoral and tibial components with postoperative coronal views. The shift length was defined by the distance between the midpoint of the components and the midpoint of both condyles (Fig 2). A radiographic outlier in the coronal view was defined as any knee alignment 4° or greater outside the ideal or any component medialization or lateralization greater than 3 mm. The ideal coronal alignment was considered to be 7° valgus with the femoral component in 7° valgus and the tibial component in neutral. Concerning the sagittal view, we surveyed the number of cases with femoral notching greater than 2 mm. A two-tailed p value of 0.05 or less was considered statistically significant. The analysis for the prevalence of radiographic outliers was completed using Fisher's exact test with a p value of 0.05 or less, which was considered to indicate a significant difference.

RESULTS

The MIS group showed higher ($p < 0.05$) postoperative extensor torque values (Fig 3A) and higher ratios of postoperative to preoperative extensor torque (Fig 3B) at 1 and 2 weeks. No differences were observed in postoperative

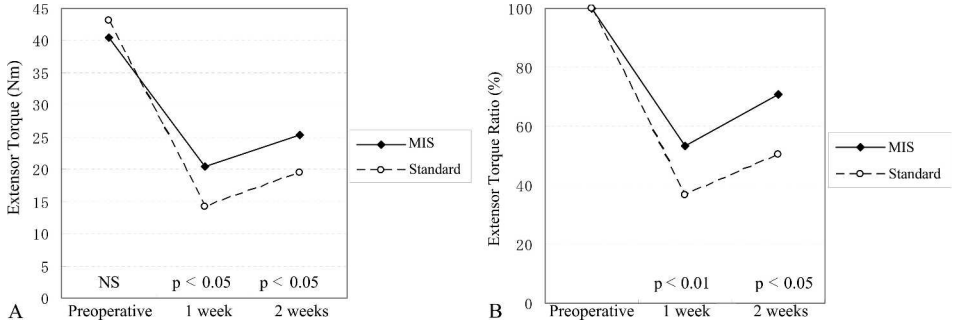

Fig 3A–B. (A) The MIS group showed higher ($p < 0.05$) extensor torque values at 1 and 2 weeks postoperatively. (B) The ratios of postoperative to preoperative extensor torque were higher in the MIS group at 1 week ($p < 0.01$) and 2 weeks ($p < 0.05$) postoperatively. NS = not significant

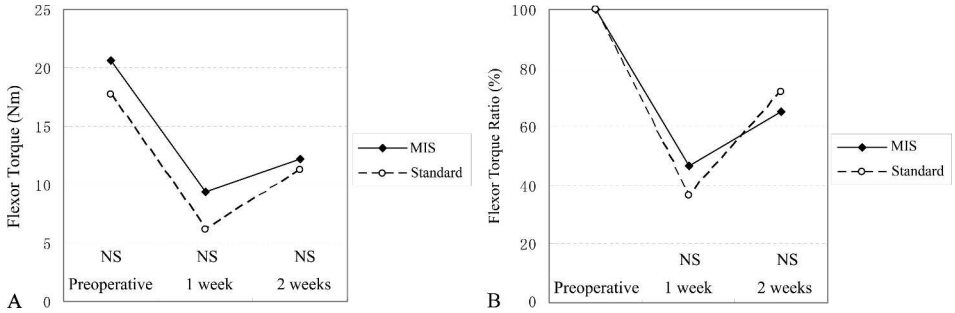

Fig 4A–B. (A) There were no differences in the flexor torque values in the two groups at 1 and 2 weeks postoperatively. (B) There were no differences in the ratios of postoperative to preoperative flexor torque in the two groups at either 1 week or 2 weeks postoperatively. NS = not significant

flexor torque values (Fig 4A) or the ratios of postoperative to preoperative flexor torque (Fig 4B) in the two groups. Preoperatively, there were no differences in the torque values of the quadriceps and hamstrings in the two groups. In the MIS group, no difference was observed between the cases with capsular only incision and those with an additional 1 to 2 cm of VMO snip in either extensor or flexor torque.

The average VAS score was lower ($p < 0.05$) in the MIS group at 1 and 2 weeks (Fig 5).

The times when the patients attained straight leg raising ($p < 0.001$), 90° knee flexion ($p < 0.001$), and T-cane gait ($p < 0.005$) were substantially earlier in the MIS group than in the standard group (Table 2).

The Knee Society functional score in the MIS group showed some advantage over the standard group at 3 weeks ($p < 0.05$) and 3 months postoperatively, but the two groups came together after 6 months. No differences in the knee scores between the two groups were found (Table 2).

We found no differences between the groups in terms of the mean postoperative femorotibial angle as assessed by the Knee Society radiographic evaluation and the alignment of the femoral and tibial components (Table 3). The assessment of the shift length of the components revealed the tibial component in the MIS group shifted to a more medial position ($p < 0.05$) (Fig 6A–B). There was no difference in the shift length of the femoral component in the two groups (Fig 6C–D). The radiographic outlier analysis (Table 4) showed more outliers in lateral shift of the tibial component in the MIS group ($p < 0.05$).

The operative time in the MIS group was longer ($p < 0.001$) than that in the standard group. We encountered no major perioperative complications in either group. One patient in the MIS group had a delay in wound healing, but this resolved within 3 weeks.

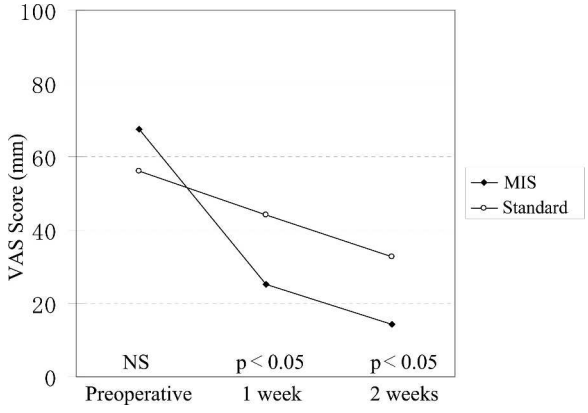

Fig 5. The average VAS score was lower ($p < 0.05$) in the MIS group at 1 and 2 weeks postoperatively. NS = not significant

DISCUSSION

The quest for less pain and quick recovery after TKA has driven patients and orthopaedic surgeons to develop MIS TKA. Although literature on this technique reports less pain, greater ROM, shorter hospitalization, and higher Knee Society scores,[2,4,8,11] there are no English reports that quantitatively show the muscle strength to support its advantages in recovery. Reports of the radiographic evaluations regarding MIS TKA are limited[1,2,6,8,11] and most of them are only in terms of alignment of the implants. We designed this study to clarify whether MIS TKA was superior to the standard medial parapatellar approach TKA for patients in recovery of muscle strength, pain level, rate of postoperative recovery, and clinical scores and whether patients who had MIS TKAs were prone to radiographically poor results, more operative time, and increased complications.

Our study was limited to a mean followup length of 16 months in the MIS group. Implant performance in the long term was not ascertained and factors that might result in early loosening because of component malposition were not addressed; therefore, longer followup would be needed before complete endorsement of MIS TKA. We believe this short followup does not affect the early postoperative outcomes, which are relevant to surgical approach. The

TABLE 2. Clinical Data

Clinical Data	MIS TKA (N = 24)	Standard TKA (N = 25)	p Value
Operative time (minutes)	152 ± 37	96 ± 16	< 0.001*
Straight leg raising (postoperative day)	1.8 ± 1.2	5.2 ± 2.1	< 0.001*
90° knee flexion (postoperative day)	5.5 ± 2.8	9.0 ± 3.8	< 0.001*
T-cane gait (postoperative day)	10.8 ± 4.9	15.4 ± 5.3	< 0.005*
Knee score at 3 weeks	87 ± 8.3	86 ± 6.7	NS
Knee score at 3 months	88 ± 8.8	86 ± 7.4	NS
Knee score at 6 months	90 ± 8.3	90 ± 6.7	NS
Knee score at 12 months	90 ± 10.0	92 ± 7.1	NS
Function score at 3 weeks	66 ± 21.2	57 ± 9.9	< 0.05*
Function score at 3 months	78 ± 15.2	72 ± 14.0	NS
Function score at 6 months	87 ± 10.8	87 ± 15.5	NS
Function score at 12 months	92 ± 10.1	91 ± 12.6	NS
Number of delays in wound healing	1	0	NS
Number of other complications	0	0	NS

Values are expressed as mean ± standard deviation; *statistically significant; MIS = minimally invasive surgery; NS = not significant

MIS group included two different techniques of capsular only incision and mini-midvastus, but no difference was observed between their results. Our clinical results were evaluated by the Knee Society knee score and functional score, but the Knee Society functional scores are poor early indicators of function after TKA. All implants in the MIS group were high flex, whereas most in the standard group were not high flex and this also could affect postoperative knee flexion; however, this should not influence assessment of muscle strength and pain level.

A comparison of the two groups in our study showed the quadriceps muscle strength in the MIS group was considerably higher than that in the standard group. We presume the reasons for this are the result of the preservation of the extensor mechanism and less pain.

In our MIS TKA, arthrotomy is performed with just a capsular incision or with an additional 1 to 2 cm of VMO snip. The patella is not everted and stretching of the patella tendon thus is reduced. According to a cadaveric study, vastus medialis muscle denervation and injury to the blood supply provided by the descending genicular artery can be avoided if the muscle split is within 4.5 cm from the patellar margin.[5]

TABLE 3. Postoperative Alignment

Parameter	MIS TKA	Standard TKA	p Value
Femorotibial angle	171.8 ± 3.4	173.2 ± 2.8	0.1
α angle	96.9 ± 2.2	97.6 ± 2.5	0.3
β angle	90.7 ± 1.6	89.5 ± 1.9	< 0.05*
γ angle	3.2 ± 2.2	3.8 ± 2.4	0.4
δ angle	85.2 ± 1.9	84.4 ± 2.4	0.2

Values are expressed as mean ± standard deviation (in degrees); *statistically significant; MIS = minimally invasive surgery

Less pain after MIS TKA also contributes to muscle strength. A comparison of the VAS scores in the two groups showed a considerable difference at 1 and 2 weeks postoperatively. The relationship between pain with muscle contraction, voluntary electrical activation, and quadriceps strength was reported in a quantified investigation.[16]

The advantage of MIS TKA is not only a smaller incision but also more rapid rehabilitation. The faster restoration of the quadriceps muscle strength and the reduced pain enable a faster return to function and contribute to an early return to their daily lives. High correlation between the quadriceps strength and functional performance was reported in a prospective study.[12] In addition, previous studies have documented MIS TKA leads to earlier gains in postoperative passive knee flexion.[2,4,8,11,17] In our study, patients in the MIS group attained straight leg raising, 90° knee flexion, and T-cane gait earlier without any major perioperative complications. A study on 40 TKAs with a medial parapatellar approach showed it took 6 months for the involved quadriceps strength to reach preoperative strength values.[12] In our study, the Knee Society scores of both groups almost came together at 6 months.

It is essential in TKA to place implants in accurate positions to achieve the best long-term implant performance and low revision rates.[15] It has been reported the mini-incision TKA using standard instruments and implants resulted in tibial component malalignment (> 4°) in four of 30 patients.[6] A retrospective comparative study showed more radiographic outliers in the quadriceps-sparing group (13 of 36 patients) than in the standard group (five of 34 patients).[4] In our series, although the β angle was 1.2° higher in the MIS group, the mean alignment of the tibial component was less than 1° varus or

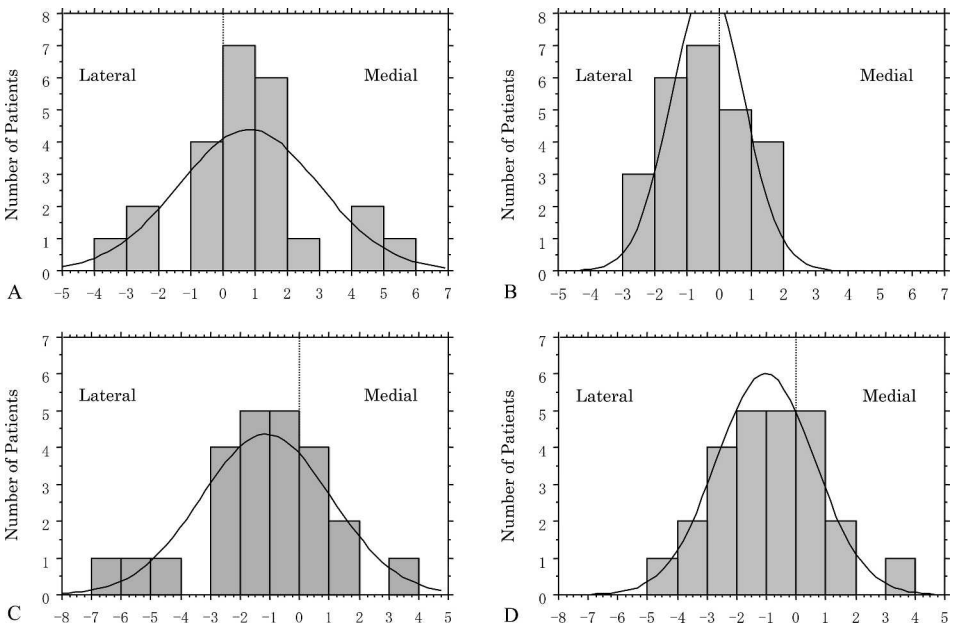

Fig 6A–D. (A) The shift lengths of the tibial components in the MIS group were 0.8 ± 2.2 mm medially. (B) The shift lengths of the tibial components in the standard group were 0.4 ± 1.1 mm laterally. The differences in the averages ($p < 0.05$) and variances ($p < 0.01$) in the two groups were significant. (C) The shift lengths of the femoral components in the MIS group were 1.1 ± 2.2 mm laterally. (D) The shift lengths of the femoral components in the standard group were 1.0 ± 1.7 mm laterally. There were no differences in the averages or the variances in the two groups.

valgus and there was no difference in the variance or the outlier analysis. After performing assessments using Knee Society radiographic evaluations, we and others[2,8,11] have not identified any component malalignment in patients. However, we should be cautious regarding the medial and lateral shift of the femoral or tibial components. Our results showed the tibial components in the MIS group shifted to a more medial position and the shift varied more widely than in the standard group. This tendency was seen mainly in our early MIS TKAs. Tibial component medialization greater than 3 mm also was reported in four of 30 quadriceps-sparing TKAs and three of 30 mini-subvastus TKAs.[1] Although tibial components in our cases ran off the medial edge only 1 to 2 mm at most, an excessive medial shift of the tibial components theoretically could increase the medial tightness or increase the risk of loosening over the long term. We suspect the medial shift of the tibial components in the MIS TKA could have resulted from difficulty in observing the lateral tibial plateau or from difficulty in clearing the lateral femoral condyle with a standard tibial implant. Surgeons should be aware of this issue.

To our knowledge, this is the first study to quantitatively evaluate quadriceps strength after MIS TKA. In our series, quadriceps strength was substantially higher at 2 weeks after MIS TKA than after standard TKA. Rehabilitation after MIS TKA was more rapid than that in standard TKA, which could be attributed to the early restoration of muscle strength. The MIS approach may result in greater difficulty in achieving proper alignment and position of the components leading to increased operative time. Nevertheless, MIS TKA is believed to contribute to preservation of quadriceps strength and reduction in postoperative pain, leading to more rapid recuperation and increased patient satisfaction.

TABLE 4. Radiographic Outlier Analysis

Number of Knees	MIS TKA (N = 24)	Standard TKA (N = 25)	p Value
Anatomic alignment outliers	5	4	NS
Femoral alignment outliers	2	4	NS
Tibial alignment outliers	0	1	NS
Femoral notch > 2 mm	3	2	NS
Lateral shift outliers in the femoral component	4	4	NS
Lateral shift outliers in the tibial component	4	0	< 0.05*

*Statistically significant; MIS = minimally invasive surgery; NS = not significant

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